UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,111	06/28/2002	Hiroshi Yanagawa	P22033	3232

7055 7590 12/16/2005

GREENBLUM & BERNSTEIN, P.L.C.
1950 ROLAND CLARKE PLACE
RESTON, VA 20191

EXAMINER	
FOSTER, CHRISTINE E	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,111	YANAGAWA ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *18-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☒ Claim(s) *1,4,5 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/28/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/28/02, 5/20/04,*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendment, filed 6/28/02, is acknowledged. Applicant is reminded that each amendment document that includes a change to an existing claim, including the deletion of an existing claim, or submission of a new claim, must include a **complete listing of all claims** ever presented (including previously canceled and non-entered claims) in the application (see MPEP 714).

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-18 in the reply filed on 10/20/05 is acknowledged. Applicant has further elected the species of **protein** as the species of target molecule, **puromycin** as the species of chemical skeleton, **biotin binding protein/biotin** as the species of combination of polypeptide and molecule, and **fluorescence imaging analysis method** as the method of measuring signal change, in accordance with the requirement for restriction set forth in the Office action mailed 9/20/05 (see also the Interview Summary mailed 10/5/05).

The traversal is on the ground(s) that the method of Group I can be considered to be analogous to the method of Group VI, as well as to the labeling agent of Group II, the immobilized protein and protein chip of Group III, the apparatuses of Groups IV and V, and the molecule or protein of Groups VII, VIII, and IX, and that therefore, the claims have unity of invention. Applicant further argues that the restriction requirement did not indicate how the claims are considered anticipated or obvious over the prior art, and that therefore, the restriction requirement fails to bear the burden of proving unpatentability.

This argument is not found persuasive because the record as clearly set forth in the office action mailed 9/20/05 demonstrated that the claims lack of unity of invention as determined under PCT Rule 13, which does not require that the claims be subject to a complete examination and shown to be unpatentable as Applicant suggests. The claims were found to lack unity of invention because the technical feature linking the inventions of Groups I-IX does not constitute a *special* technical feature, as the technical feature does not define a contribution over the prior art (see p. 3 of the office action in particular).

The requirement is still deemed proper and is therefore made FINAL.

Applicant indicated that claims 1-18 are generic, and that claims 1-18 are readable upon the elected species (p. 8). However, the examiner has determined that claim 18 does not read upon the elected species of **fluorescence imaging analysis method** since it recites fluorescence depolarization and fluorescence correlation spectroscopy, but not fluorescence imaging analysis. Therefore, claim 18 is hereby withdrawn from examination. Claims 18-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Applicant also requested rejoinder of the claims upon allowance of the elected claims. Withdrawn claims may be rejoined in cases where the Examiner has required restriction between product and process claims and *where applicant elects claims directed to the product.* In such cases, when a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Since Applicant has elected process claims for prosecution, rejoinder of the withdrawn claims is not appropriate. See MPEP § 821.04 and "Guidance on

Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Priority

Acknowledgment is made of the present application as a proper National Stage (371) entry of PCT Application No. PCT/JP00/05920, filed 8/31/00, which claims priority under USC 119 to Japanese document 11244704, filed 8/31/1999. A copy of the priority document has been received from the international bureau.

Information Disclosure Statement

Applicant's Information Disclosure Statements filed 6/28/02, 5/20/04, and 2/20/05 have been received and entered into the application. The documents have been considered by the Examiner as indicated on the attached forms PTO-1449. Documents number 2717499 by Weiss et al. as cited on the IDS of 2/20/05 and the document by Perran et al. on the IDS of 6/28/02 were not considered because they are French language documents. Regarding document 10-320093 cited on the IDS of 6/28/02, only the translation supplied has been considered.

Claim Objections

1. Claims 1, 4-5, and 11 are objected to because of the following informalities:

2. Claim 1 contains a grammatical error in part (2) ("...which is caused an interaction...").

3. Claim 1 recites a "molecule" in the preamble, and later recites "a target molecule" in part (1). It is presumed that a single molecule is being referred to; if this is the case, the preamble may be amended for consistency to recite "a target molecule".

4. Claim 4 appears to require an article such as "a" before "fluorescence labeling agent".

5. The word "combination" in line 3 of claim 11 should apparently be pluralized for subject-verb agreement.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed. Factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application are listed in the MPEP. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional

characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." MPEP 2163.

Claim 6 recites an acceptor moiety comprising a compound containing "a chemical skeleton" of the elected species of puromycin, or an "analog" of said compound. The claims are therefore drawn to compounds comprising **a** chemical skeleton of puromycin or analogs of such compounds. However, the specification does not describe the structure of the various "chemical skeletons" of puromycin, or provide a definition of what would constitute a chemical skeleton of puromycin. In addition, the specification does not describe compounds that are "analogs" of those that comprise such chemical skeletons. It is unclear what portions of the puromycin chemical skeletons could be altered without affecting the function of having the ability to bind to the C-terminus of a protein. For one to be in possession of the claimed invention, the inventor would have to know the functional consequences of structural alterations. Thus due to the limited predictability in the art, a skilled artisan would not find adequate support for the genus of compounds containing "chemical skeletons" of puromycin and analogs of such compounds.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 1 recites detecting a change of a signal "which is caused [by] an interaction between the C-terminus labeled protein and the target molecule among signals generated by the

C-terminus labeled protein or the target molecule". There is no antecedent basis for "signals generated by the C-terminus labeled protein or the target molecule" in the claim. It is also unclear what the clause "among signals generated..." refers back to—to "detecting a change" or to "an interaction"?

11. Claim 1 recites a "C-terminus labeled" protein. The term is indefinite because it is not defined in the specification, such that the metes and bounds of the claim are not adequately defined. The "C-terminus" of the protein could refer to the C-terminal residue or to a C-terminal domain or region, such as the C-terminal half of the protein.

12. In claim 5, it is unclear due to the sentence structure what the phrase "to allow protein synthesis" refers to. For example, is the transcription and/or translation system allowing for protein synthesis? Or is protein synthesis to occur in the presence of a labeling agent?

13. Claim 5 recites a labeling agent which comprises a labeling moiety comprising a labeling substance and an acceptor moiety...". It is unclear what the "acceptor moiety" refers back to in the sentence. Is the reaction "in the presence of" the labeling agent and the acceptor moiety? Or does the labeling moiety comprise the labeling substance and the acceptor moiety? It is unclear from the sentence structure how these substances are related. The claim has been interpreted as referring to reaction in the presence of a labeling agent, which comprises a labeling moiety, which in turn comprises a labeling substance, and in the presence of an acceptor moiety, which comprises a compound having an ability to bind to the C-terminus of a protein.

14. Claim 7 recites a compound "in which the labeling moiety binds to the acceptor moiety via a spacer". It is unclear whether this is an active process step in which the labeling moiety binds to the acceptor moiety during the performance of the method, or whether it is simply a

description of the compound structure, i.e. that the compound is made up of a labeling moiety that is bound via a spacer to the acceptor moiety.

15. Claim 9 recites the limitations "the labeled moiety" and "the labeled moiety which constitutes said protein". There is insufficient antecedent basis for these limitations in the claim. In addition, the term "constitutes" is vague and indefinite as it is unclear in what sense the labeling moiety "constitutes" the protein.

16. Claim 9 recites that the C-terminus labeled protein is bound to the solid phase "at" the labeled moiety or at a moiety other than the labeled moiety. The claim is unclear--is the protein bound to the solid phase via the moiety, i.e., is the interaction with the solid phase mediated by atoms of the moiety? Or is the protein bound to the solid phase in the same position as the moiety?

17. Claims 10, 13 and 15 also recite the limitation "the labeled moiety constituting the protein". There is insufficient antecedent basis for this limitation in the claims. It is also unclear how the labeled moiety "constitutes" the protein as discussed above.

18. Claim 16 recites the limitation "the labeled molecule". There is insufficient antecedent basis for this limitation in the claims.

19. Claim 17 recites the limitations "the labeled moiety of the C-terminus labeled protein" and "the signal generated from the labeled moiety of the C-terminus labeled protein". There is insufficient antecedent basis for these limitations in the claims. There is no prior mention that the signal is generated from the C-terminus labeled protein.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

21. Claims 1-3, and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Casey et al. ("Purification of bacterially expressed single chain Fv antibodies for clinical applications using metal chelate chromatography" (1995) *Journal of Immunological Methods* **179**:105-116).

Casey et al. teach a method for analyzing an interaction between a protein a molecule, comprising the steps of bringing a C-terminus labeled protein (the anti-CEA antibody MFE-23 His that is labeled with a C-terminal hexa-histidine tag) into contact with a target molecule (CEA) and detecting a change of a signal (^{125}I activity) which is caused by the interaction between the anti-CEA antibody and the CEA target molecule (see the abstract; Figure 1; the paragraph bridging p. 106-107; and p. 110, section 2.11 in particular).

With regard to claim 2, the target molecule CEA is a protein.

With regard to claim 3, the target molecule CEA is coupled to Sepharose 4B chromatography medium, which has been interpreted as a "labeling substance" (see p. 109, section 2.7).

With regard to claim 8, the target molecule is bound to a solid phase (Sepharose 4B) (see sections 2.7 and 2.11).

With regard to claims 9, the C-terminus labeled protein (anti-CEA antibody) is bound to the CEA-coupled Sepharose 4B solid phase when it interacts with the target molecule CEA (see section 2.11). It is unclear what "the labeled moiety" or "a moiety other than the labeled moiety which constitutes said protein" refers to (see rejection under 112, 2nd paragraph above), but the CEA target molecule is "labeled" as discussed above, it would seem to constitute a "labeled moiety". The C-terminus labeled anti-CEA antibody is bound to the solid phase via the labeled moiety. With regard to claim 10, the anti-CEA antibody comprises a molecule having an ability to specifically bind to a particular polypeptide (CEA), wherein the molecule is bound to the solid phase via a linkage with CEA bound to the surface of the solid phase. As discussed above, the binding of anti-CEA to solid phase-bound CEA in the affinity chromatography method above anticipates this limitation.

22. Claims 1-2 and 5-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Lohse et al. (US 6,660,473 B1, which claims priority to provisional application No. 60/143,339, filed on Jul. 12, 1999).

Lohse et al. teach a method for analyzing an interaction between a protein a molecule, comprising the steps of bringing a C-terminus labeled protein into contact with a target molecule and detecting a change of a signal which is caused by the interaction between the C-terminus labeled protein and the target molecule (see in particular the abstract and column 1, lines 42-45; column 7, lines 6-67 column 3, lines 7-19; and column 8, lines 19-24 and 35-37). In particular, Lohse et al. analyzing the interaction between a C-terminally tagged myc peptide with an anti-

myc monoclonal antibody and subsequently with NeutrAvidin (column 7, lines 36-67), and well as the interaction between C-terminally tagged fibronectin type II (fn3) with NeutrAvidin protein (column 8, lines 1-24). The change associated with the interaction between C-terminus labeled protein and target molecule is detected through phosphorimaging by detecting a change in the radiolabel associated with the C-terminus labeled protein (column 7, lines 64-67; column 8, lines 21-24). Although Lohse et al. do not specifically teach that the NeutrAvidin or anti-myc antibodies are considered to be "target molecules," the teaching is anticipatory since the method of Lohse et al. teaches all active process steps of claim 1.

With regard to claim 2, Lohse et al. teach NeutrAvidin protein (column 8, lines 21-24).

With regard to claims 5-6, the C-terminus labeled protein is prepared by expressing a nucleic acid comprising a coding region for the protein in an *in vitro* transcription and translation system to allow protein synthesis in the presence of a labeling agent (puromycin tag) which comprises a labeling moiety comprising a labeling substance (such as a detectable label or chemically reactive functional group) and an acceptor moiety (such as puromycin or its derivatives) comprising a compound having an ability to bind to the C-terminus of a protein (column 1, lines 43-45 and 59-65; column 2, lines 25-37; column 3, line 63 to column 4, line 53; and column 5, lines 1-31). In particular, Lohse et al. teach a system of *in vitro* transcription of dsDNA followed by *in vitro* translation of the produced mRNA (see column 7, lines 45-55 and column 8, 14-19; column 4, lines 10-14). The translation system is stalled and the labeling agent (puromycin tag) is added.

With regard to claim 7, Lohse et al. teach labeling agents (puromycin tags) that comprise a compound in which the labeling moiety (tag) is bound to the acceptor moiety (puromycin) via a

spacer (nucleotide sequence of 1-200 nucleotides that is positioned between the tag and the puromycin (column 2, lines 16-20; column 4, lines 28-36 and Figures 4-6).

With regard to claim 8, NeutrAvidin is attached to a solid phase (microscope slide or chip surface) (column 7, lines 61-63 and column 8, lines 21-24). In other embodiments, interactions between C-terminus labeled antibodies and immobilized antigens can be detected (Figure 2 and column 41, lines 27-30). Alternatively, Lohse et al. also that the C-terminus labeled protein can be attached to a solid phase (see in particular column 4, lines 50-53).

With regard to claims 9-11, it is not clear what the "labeled moiety" is or to which molecule the moiety is attached (see rejection under 112, 2nd paragraph above). However, with analogy to the "labeling moiety" recited in claim 5, the "tag" moiety of the puromycin tags of Lohse et al. would seem to fit this description. Lohse et al. teach that the myc peptide and Fn3 C-terminus labeled proteins are labeled with Biotin-TEG-dCdC-puromycin labeling agent, such that the C-terminus labeled protein is bound to the solid phase via the biotin moiety, which interacts with immobilized biotin-binding protein (NeutrAvidin). Other biotin-binding proteins are taught (column 1, lines 17-20).

23. Claims 1-9 and 12-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Szostak et al. (US 6,258,558 B1).

Szostak et al. teach a method for analyzing an interaction between a protein and a molecule, comprising bringing a C-terminus labeled protein ("RNA-protein fusion") (see column 11, line 41 to column 12, line 16; column 13, line 43 to column 14, line 3; and Figure 1C) into contact with a target molecule (column 42, lines 20-38 and line 55 to column 43, line 23; column 14, line 33 to column 15, line 29; column 41, lines 4-57; and Figure 2 in particular). The C-

terminus labeled protein of Szostak et al. is a protein which is covalently linked to an mRNA molecule via the protein C-terminus (column 11, lines 52-55 in particular).

In specific embodiments, Szostak et al. teach contacting a C-terminus labeled protein which is a myc peptide with an anti-myc antibody (column 22, line 50 to column 23, line 7 and Figure 11; column 30, lines 32-60). Szostak et al. further teach the step of detecting a change of a signal caused by this interaction by detecting a change in the radiolabel by denaturing PAGE (column 30, lines 47-65 and Figure 11). Alternatively, the interaction of a C-terminus labeled protein with an oligonucleotide affinity target compound (dT25) can be detected by scintillation counting of the radiolabeled protein (column 32, line 10 to column 33, line 2; column 23, lines 24-39).

Other types of interactions that may be analyzed involve immobilizing the C-terminus labeled protein onto a DNA chip (column 42, line 55 to column 44, line 14), in which the chip with displayed C-terminus labeled protein may be analyzed for interaction with a detectably labeled target molecule, in this case a probe protein (see column 43, lines 7-16). The interaction is then detected by imaging spots on the chip that become fluorescently labeled due to the binding of the probe protein.

With regard to claims 2-4, the target molecule (probe protein above) may labeled with a fluorescent dye.

With regard to claims 5-6, the C-terminus labeled protein is prepared by *in vitro* or *in situ* expression (translation) of mRNA comprising a coding region of the protein in a translation system to allow protein synthesis in the presence of a labeling agent which comprises a labeling moiety comprising a labeling substance (the labeling moiety is considered here to be the mRNA

molecule) and an acceptor moiety comprising a compound (puromycin) having the ability to bind to the C-terminus of the protein (column 11, line 40 to column 12, line 1; Figure 1B and 1C). The mRNA molecule is first ligated to a puromycin-tethered oligo in the presence of a DNA splint, forming the "labeling agent" (Figure 1B). Translation of the protein proceeds, and then the puromycin acceptor moiety attaches to the protein, labeling the protein at the C-terminus (Figure 1C).

With regard to claim 7, the mRNA molecule binds to the acceptor moiety (puromycin) indirectly by way of the DNA "splint" (column 13, lines 43-50 and Figure 1B). The oligo to which the puromycin is tethered would also be considere to be a "spacer" separating the mRNA and the puromycin (Figure 1B).

With regard to claim 8, the C-terminus labeled protein may be bound to a solid phase (DNA chip) as discussed above (column 42, line 55 to column 44, line 14).

With regard to claim 9, the C-terminus labeled protein can be bound to a solid phase (DNA chip) via the mRNA molecule to which it is fused (see column 42, line 58 to column 43, line 3). That is, the DNA chip has immobilized DNA molecules that are capable of annealing to the mRNA label on the C-terminus labeled protein, thereby immobilizing the protein on the chip. The mRNA molecule in this case would seem to be the "labeled moiety" in this case.

With regard to claim 12, the teaching of detecting the location of fluorescent dye on a DNA chip (column 43, lines 7-16) would inherently comprise fluorescence "imaging" since fluorescence is an optically visible property. One skilled in the art would immediately envisage that the detection of fluorescently labeled probe proteins bound to a chip would involve a method of "imaging" of the fluorescent signal.

With regard to claim 13-14, Szostak et al. teach that the C-terminus protein is bound to the solid phase via the labeled moiety (mRNA molecule), which would seem to "constitute" the protein since it is attached to the protein. The target molecule (probe protein) is labeled with a labeling substance, and the change of the fluorescence signal would inherently comprise "imaging," as discussed above.

24. Claims 1-2 and 5-9 rejected under 35 U.S.C. 102(e) as being anticipated by Yanagawa et al. (US 6,361,943 B1). This rejection is being made because the priority document in the instant application is a Japanese language document.

The applied reference has a common inventors and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Yanagawa et al. teach a method for analyzing an interaction between a protein and a molecule, comprising bringing a C-terminus labeled protein (a protein bound to the 3' end of a nucleic acid molecule; see column 4, lines 35-43 and Figure 4 in particular) into contact with a target molecule, such as nucleic acid or protein (column 7, lines 33-40; column 16, line 60 to column 17, line 58; and Example 3). Yanagawa et al. further teach detecting a change of a signal caused by the above interaction, for example by ELISA (column 17, lines 26-31) or by PCR methods (column 27, lines 5-28). It is noted that ELISA is an example of a suitable detection method according to the instant invention.

With regard to claim 2, the target molecule may be nucleic acid, protein, saccharides, or lipids (column 17, lines 19-21).

With regard to claim 5, the C-terminus labeled protein is prepared by transcribing DNA into an RNA transcript, which is then translated in a cell-free translation system to allow protein synthesis in the presence of a labeling agent (see Figure 2). The labeling agent in this case is the RNA transcript. The acceptor moiety is a nucleoside or a substance having a chemical structure analagous to a nucleoside, which can be covalently bonded to an amino acid (column 5, lines 28-57).

With regard to claim 6, the acceptor moiety may comprise puromycin (see claim 1).

With regard to claim 7, Yanagawa et al. teach that the RNA transcript may be attached to the acceptor moiety via a DNA spacer (Figure 4).

With regard to claim 8, Yanagawa et al. teach that the target molecules may be bound to a microplate, beads or the like (column 17, lines 19-32). In one embodiment, a microplate is coated with the target molecule IgG (column 27, lines 5-9).

With regard to claim 9, Yanagawa teach that the C-terminus labeled protein is bound to the solid phase via interaction between the label (ZZ region of protein A) and the immobilized target molecule.

Claim Rejections - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lohse et al. in view of Rothschild et al. (US 6,303,337 B1).

Lohse et al. is as discussed above, which teaches methods for analyzing interactions between a C-terminus labeled protein and a target molecule, such as an anti-myc antibody. Lohse et al. further teach that the C-terminus labeled protein can be attached to a solid phase (see in particular column 4, lines 50-53 and Figure 9). However, Lohse et al. do not specifically teach a method for analyzing an interaction where the C-terminus labeled protein is bound to the solid phase and *wherein the change of signal is detected by fluorescence imaging analysis*, as recited in claims 15-16. Lohse et al. also teach an embodiment wherein the target molecule (anti-myc antibody or NeutrAvidin) is bound to the solid phase (protein A sepharose or microscope slide/chip, respectively) but fail to specifically teach that *the change of signal is detected by fluorescence imaging analysis* as recited in claim 17. In the specific examples provide in Lohse et al., the interactions are detected by phosphorimaging of radiolabel associated with the labeled protein.

Rothschild et al. teach proteins labeled with detectable markers, which can be bound to solid phases either via a second label that acts as an affinity marker for interaction with the solid phase, or via non-specific binding (see in particular column 9, lines 15-35; column 8, lines 3-21), and which can be analyzed for interaction with antibodies by fluorescence imaging analysis of the fluorescent dye-conjugated antibody (column 28, lines 54-65; column 30, lines 16-32). In particular, Rothschild et al. teach that the labeled protein may be immobilized on streptavidin-coated beads or plates and then contacted with antibodies conjugated to fluorescent dyes. Rothschild et al. further teach that non-radioactive labels such as fluorescent markers do not have the drawbacks associated with radioactive labels, and that radioactive labels do not provide a simple and rapid means of studying the interaction of nascent proteins with other molecules (see column 3, lines 55-60; "nascent" in this context refers to proteins that have been translated in a translation system (see column 6, lines 35-62; column 15, lines 1-38). Other drawbacks associated with radioactive labels include potential risk and waste disposal issues (column 3, lines 3-55).

Therefore, it would have been obvious to one of ordinary skill in the art to detect the interaction between the C-terminus labeled protein of Lohse et al. with the anti-myc antibody by fluorescent imaging of the fluorescent dye-conjugated antibody binding to a solid-phase bound protein, as taught by Rothschild et al., rather than by detection of a radiolabel, since Rothschild et al. teach that radioactive labels are undesirable for simple and rapid analysis of the interactions of nascent proteins with other molecules. One would have reasonable expectation of success because Lohse et al. teach that the C-terminus labeled protein may be bound to streptavidin-coated solid phases (column 1, lines 13-21; column 5, lines 12-14).

It would have been further obvious to detect the interaction between the C-terminus labeled protein and the solid-phase bound target molecule NeutrAvidin as in Lohse et al. by using fluorescence imaging analysis of a fluorescently labeled C-terminus protein as taught by Rothschild et al. because Rothschild et al. teach the benefits of fluorescent vs. radioactive labels. One would have reasonable expectation of success because while the specific examples of Lohse et al. teach that the C-terminus protein is radiolabeled, other C-terminus labeled proteins are taught that bear fluorescent labels (Figure 5 in particular). It is unclear what is meant by "the labeled moiety of the C-terminus labeled protein" (see rejection under 112, 2nd paragraph above); however, since the fluorescent labels of Lohse et al. are part of the C-terminal label, this would appear to meet the limitation.

28. Claim 1 is rejected under 35 U.S.C. 103(a) as being obvious over Yanagawa et al. (US 6,228,994 B1) in view of Szostak et al.

The applied reference has a common inventors and a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a

terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Yanagawa et al. teach a method for analyzing an interaction between a C-terminus labeled protein and a molecule (protein or nucleic acid) (column 1, line 64 to column 2, line 4; column 2, lines 48-55; and column 7, lines 17-25). Yanagawa et al. fail to recite the specific steps of contacting the labeled protein with the target molecule and detecting a change of a signal caused by the interaction.

Szostak et al. (discussed above) teach methods for analyzing an interaction between a C-terminus labeled protein and target molecules, in which the target molecule is contacted with the C-terminus labeled protein and the interaction is detected by detecting a change of signal, for example a fluorescent signal associated with a labeled target molecule (probe protein) (column 41, lines 4-56 and column 42, line 55 to column 44, line 22).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the steps of contacting the interacting molecules and detecting the interaction, as taught in Szostak et al., in the method for analyzing an interaction of Yanagawa et al. because Szostak et al. teach that such steps are an appropriate format for detecting interactions between C-terminus labeled proteins and interacting molecules. One would have reasonable expectation of success because the method of Yanagawa et al. is generic and simply does not recite specific steps associated with the method. One skilled in the art would recognize that such steps, as those of Szostak et al., would be associated with a method of assaying intermolecular interactions, such as that of Yanagawa et al.

Double Patenting

29. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

30. Claims 1-2 and 5-7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,361,943 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because U.S. Patent No. 6,361,943 also recites a method for assaying interaction between a C-terminus labeled protein and a protein or nucleic acid molecule. The claimed labeled proteins of '943 are seen to be inherently C-terminus labeled in the context of the specification, for example at Figure 4. It would be immediately envisaged by skilled in the art would recognize that they "assay step" recited in claim 21 of '941 for assaying protein/protein or protein/nucleic acid intermolecular action would inherently comprise the steps of contacting the interacting molecules and detecting a change of a signal in order to assay the interaction.

Conclusion

31. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kuimelis et al. (US 6,537,749) also teach methods for detecting interactions involving C-terminus labeled proteins which are RNA-protein fusions, as in Szostak et al. (discussed above).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christine Foster, Ph.D.
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

12/12/05